REMARKS

Claims 24-28 have been canceled, without prejudice and claims 29-32 have been amended. Support for these amendments can be found throughout the specification and claims as originally filed. Specifically, support may be found, for example, at page 83, lines 1-2. Claims 29-33 will be pending upon entry of the instant amendment.

No new matter has been added by way of amendment, and Applicants submit that the application is now in condition for allowance.

The Rejection of Claims 24 and 29 under 35 U.S.C. §112, Second Paragraph Should Be Withdrawn

Claims 24 and 29 were rejected by the Examiner under 35 U.S.C §112, second paragraph, because the term "modulate" purportedly "renders the claim indefinite". Applicants respectfully traverse this rejection and submit that the term "modulate" does not render the claims indefinite as the term is well defined within the specification. According to the specification, the term "modulate" means to either inhibit or stimulate (refer to, for example, page 4, line 28; and page 58, line 6). Applicants submit that this term is not only well defined within the specification, but is also definite as it provides for only two options – to either stimulate or inhibit. The term modulate is therefore not ambiguous. Applicants therefore respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. §112, second paragraph rejection over claims 24 and 29.

The Rejection of Claims 24-33 under 35 U.S.C. §112, Second Paragraph Should Be Withdrawn

Claims 24-33 were rejected by the Examiner under 35 U.S.C §112, second paragraph, because the term "modulating apoptosis" purportedly "renders the claim indefinite". Applicants respectfully traverse this rejection and submit that the term "modulates apoptosis", as discussed above, does not render the claims indefinite as the term modulate is well defined within the specification. Accordingly, the term "modulates apoptosis" means to either "inhibit or stimulate" apoptosis. Applicants submit that this term is not only well defined within the specification, but is also definite as it provides for only two options – to either stimulate or inhibit apoptosis. The term modulates apoptosis is therefore not ambiguous.

The Examiner additionally states that "[i]t is unclear what the limitations of "modulating apoptosis" are because the specification does not define the compound". Applicants respectfully disagree and submit that defining the compound is not necessary for the claim to be definite as the claims are directed at methods of identifying a compound capable of modulating apoptosis. Applicants state in the specification that such compounds may be, for example, small molecules, peptides or antibodies. Applicants submit that this is a sufficient description of the compound used in the claims as one of skill in the art would screen libraries of compounds, i.e. small molecules, to identify ones that are capable of modulating apoptosis. Applicants submit that such methods are common practice in the Pharmaceutical industry and that it would be overly burdensome for Applicants to define all of the compounds present in libraries used to screen for modulators. However, on page 82, lines 15-29 of the specification (see below), Applicants define the term compound and further provide a description of compounds which are considered stimulatory agents vs. those that are considered inhibitory agents.

> The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of programmed cell death-related polypeptide activity associated with the cell. An agent or compound that modulates programmed cell death-related polypeptide activity can be an agent or compound as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of a programmed cell death-related polypeptide, a peptide, a programmed cell death-related peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more of the biological activities of programmed cell death-related polypeptide. Examples of such stimulatory agents include active programmed cell death-related polypeptide and a nucleic acid molecule encoding a programmed cell death-related polypeptide that has been introduced into the cell. In another embodiment, the agent inhibits one or more of the biological activities of programmed cell death-related polypeptide. Examples of such inhibitory agents include antisense programmed cell death-related nucleic acid molecules and anti-programmed cell death-related polyeptide antibodies.

Applicants additionally submit that the identification of modulators of apoptosis is desirable because in some instances, one may want to identify compounds capable of stimulating apoptosis, whereas in other instances one may want to identify compounds capable of inhibiting apoptosis. Applicants provide examples of situations when it is desirable to identify inhibitors rather than stimulators (refer to page 83, lines 5-18 – see below).

> In one embodiment, the method involves administering an agent (e.g., an agent identified by a screening assay described herein), or a combination of agents, that modulates (e.g., upregulates or downregulates) programmed cell death-related expression or activity. In another embodiment, the method involves administering a programmed

> cell death-related polypeptide or nucleic acid molecule as therapy to compensate for reduced or aberrant programmed cell death-related expression or activity.
>
> Stimulation of programmed cell death-related activity is desirable in situations in which a programmed cell death-related polypeptide is abnormally downregulated and/or in which increased programmed cell death-related activity is likely to have a beneficial effect. Conversely, inhibition of programmed cell death-related activity is desirable in situations in which programmed cell death-related activity is abnormally upregulated and/or in which decreased programmed cell death-related activity is likely to have a beneficial effect.

Applicants therefore submit that the term "modulates apoptosis" is definite. Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. §112, second paragraph rejection over claims 24-33.

The Rejection of Claims 24-28 under 35 U.S.C. §112, First Paragraph Should Be Withdrawn

Claims 24-28 were rejected by the Examiner under 35 U.S.C §112, first paragraph, because the term "95% identity" is considered new matter by the Examiner. Applicants respectfully traverse this rejection, however in an effort to expedite prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have canceled claims 24-28, thereby rendering the Examiner's rejection moot. Applicants therefore respectfully request withdrawal of the foregoing 35 U.S.C. §112, first paragraph rejection over claims 24-28.

The Rejection of Claims 24-28 under 35 U.S.C. §112, First Paragraph Should Be Withdrawn

Claims 24-28 were rejected by the Examiner under 35 U.S.C §112, first paragraph, as failing to comply with the written description requirement because the Examiner considers that the specification does not provide written description support for the term "95% identity". Applicants respectfully traverse this rejection, however in an effort to expedite prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have canceled claims 24-28, thereby rendering the Examiner's rejection moot. Applicants therefore respectfully request withdrawal of the foregoing 35 U.S.C. §112, first paragraph rejection over claims 24-28.

The Rejection of Claims 24-28 under 35 U.S.C. §112, First Paragraph Should Be Withdrawn

Claims 24-28 were rejected by the Examiner under 35 U.S.C §112, first paragraph, because "The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims". Specifically, the Examiner is of the opinion that the specification is non-enabling for the term "95% identity". Applicants respectfully traverse this rejection, however in an effort to expedite prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have canceled claims 24-28, thereby rendering the Examiner's rejection moot. Applicants therefore respectfully request withdrawal of the foregoing 35 U.S.C. §112, first paragraph rejection over claims 24-28.

The Rejection of Claims 24, 25, 28-30 and 33 under 35 U.S.C. §112, First Paragraph Should Be Withdrawn

Claims 24, 25, 28-30 and 33 were rejected by the Examiner under 35 U.S.C §112, first paragraph, because "The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims". Specifically, the Examiner is of the opinion that the specification is "[e]nabling for a method for identifying a compound capable of modulating apoptosis comprising a sample wherein the sample comprises a brain cell or neuron expressing the polypeptide, does not reasonably provide enablement for a method for identifying a compound capable of modulating apoptosis comprising a sample wherein the sample comprises a cell expressing the polypeptide."

Applicants respectfully traverse this rejection. Contrary to the Examiner's assertion, Applicants submit that even though the data presented within the specification demonstrates expression of the molecule of the invention in brain cells and neurons, one of skill in the art could, as described throughout the present application, recombinantly express the gene in cells other than brain cells or neurons and perform the claimed *in vitro* methods (refer to, for example, page 39, lines 9-13 and page 41, line 7 to page 45, line 5). Applicants submit that recombinantly expressing the gene of the present application in host cells in order to perform the claimed *in vitro* method does not constitute undue experimentation as such methods are common practice. (emphasis added).

Applicants therefore respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. §112, first paragraph rejection over claims 24, 25, 28-30 and 33.

The Rejection of Claims 24-33 under 35 U.S.C. §112, First Paragraph Should Be Withdrawn

Claims 24-33 were rejected by the Examiner under 35 U.S.C §112, first paragraph, because the term "cell" is considered new matter by the Examiner as the term reads on both *in vitro* and *in vivo* methods. Applicants respectfully traverse this rejection, however in an effort to expedite prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have canceled claims 24-28 and amended claim 29 to read "An *in vitro* method" as suggested by the Examiner, thereby rendering the Examiner's rejection moot. Applicants therefore respectfully request withdrawal of the foregoing 35 U.S.C. §112, first paragraph rejection over claims 24-33.

The Rejection of Claims 24-33 under 35 U.S.C. §112, First Paragraph Should Be Withdrawn

Claims 24-33 were rejected by the Examiner under 35 U.S.C §112, first paragraph, "[b]ecause the specification, while being enabling for a method for identifying a compound capable of modulating apoptosis in cell culture (*in vitro*), does not reasonably provide enablement for a method for identifying a compound capable of modulating apoptosis *in vivo*." Applicants respectfully traverse this rejection, however in an effort to expedite prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have canceled claims 24-28 and amended claim 29 to read "An *in vitro* method", thereby rendering the Examiner's rejection moot. Applicants therefore respectfully request withdrawal of the foregoing 35 U.S.C. §112, first paragraph rejection over claims 24-33.

The Rejection of Claims 24-33 under 35 U.S.C. §112, First Paragraph Should Be Withdrawn

Claims 24-33 were rejected by the Examiner under 35 U.S.C §112, first paragraph, because "The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims". Specifically, the Examiner states that "[a]n assay comprising a single cell or insufficient amount of cells would yield undetectable results". Applicants respectfully traverse

this rejection, however in an effort to expedite prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have canceled claims 24-28 and amended claims 29-32 to read "cells", thereby rendering the Examiner's rejection moot. Applicants therefore respectfully request withdrawal of the foregoing 35 U.S.C. §112, first paragraph rejection over claims 24-33.

CONCLUSION

In view of the amendments and remarks made herein, Applicants respectfully submit that the rejections presented by the Examiner are now overcome and that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is believed that this paper is being filed timely and that a three month extension of time is required. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

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MILLENNIUM PHARMACEUTICALS, INC.

By Tracy M. Sioussat

Tracy M. Sioussat
Reg. No. 50,609
40 Landsdowne Street
Cambridge, MA 02139
Telephone: (617) 374-7679
Facsimile - (617) 551-8820